

## **REMARKS**

### **Claim Status**

Claim 40 has been amended to incorporate the subject matter of claim 47, which has been subsequently cancelled. Claims 41 and 49 have been amended to reflect the new dependencies due to the cancellation of claim 47.

In addition, claims 40 has also been amended to read “wherein said replacement results in one or more amino acid substitutions” for the purpose of improving clarity.

Claim 44 has been amended to recite that the one or more point mutations result in at least one amino acid substitution of Asp165 to Gly. Support for this amendment is found at least in Table 2, on pages 16-20 of the instant specification, which provides eight exemplary variants: Cry3Bb.11032, Cry3Bb.11035, Cry3Bb.11046, Cry3Bb.11057, Cry3Bb.11081, Cry3Bb.11082, Cry3Bb.11084 and Cry3Bb.11098. Detailed analysis of the support in Table 2 is presented in the following 35 U.S.C. §112, first paragraph, rejection section.

Claim 46 has been amended to recite that the point mutation at position 311 is Ser311 replaced by leucine.

Furthermore, claims 44 and 46 have been amended to improve clarity by inserting the word “modified” in front of the word “polypeptide”.

Claims 38 and 39 have been cancelled.

New claims 50-54 have been added to refer to the specific exemplary variants of the modified Cry3Bb\* polypeptides that are listed in Table 2, on pages 16-20 as well as described in Section 6.0, titled “Brief Description of the Sequence Identifiers”, on pages 191-194 of the instant specification.

Pursuant to 37 C.F.R. §1.118(a), Applicants respectfully submit that the above amendments do not introduce any new material into the application. With the present amendments, there are 14 claims pending, namely, claims 40-46 and 48-54.

**Rejection under 35 U.S.C. § 112, first paragraph (Written Description)**

Claims 38-49 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Examiner states that the phrase “one or more point mutations ... Gln348 to arginine” in claims 38, 39 and 46; the phrase “one or more point mutations ... Lys189 to Gly” in claim 44; and the phrase “one or more amino acid ... lysine or valine” in claim 40 are not supported in the instant specification or the originally filed claims and that such phrases constitute new matter. Applicants respectfully traverse this rejection.

With respect to the phrase “one or more point mutations ... Gln348 to arginine” in claims 38, 39 and 46, Applicants submit that claims 38 and 39 have been cancelled and that claim 46 does not recite this phrase.

With respect to the phrase “one or more point mutations ... Lys189 to Gly” in claim 44, Applicants submit that claim 44 as presently amended no longer recites this phrase, instead, recites a different phrase “one or more point mutations result in at least one amino acid substitution of Asp165 to Gly”. As presented in Applicants’ previous response, the instant specification describes modifications of wild-type Cry3Bb nucleotides at one or more sites, which result in a change in one or more amino acid residues in the modified crystal proteins. Such one or more sites could be in helices regions, for example,  $\alpha$  helix 4 region. Claim 44 refers to a modified Cry3Bb\* polypeptide comprising one or more modifications at one or more

sites in or near  $\alpha$  helix 4, which result in at least one amino acid substitution of Asp165 to Gly. Applicants herewith re-submit the Table of Support that was presented in the previous response of December 13, 2005, which clearly and unambiguously demonstrates the written support for the phrase “one or more point mutations result in at least one amino acid substitution”.

**Table of Support**

<b>Places in the Specification</b>	<b>Citation</b>
Page 15, lines 3-8	... at least one, and preferably, more than one, and most preferably, a significant number, of wild-type <i>cry3</i> nucleotides have been <b>replaced with one or more</b> nucleotides, or where <b>one or more</b> nucleotides have been <b>added to or deleted</b> ...
Page 22, line 6-7;  line 19-20;  lines 22-25;  lines 28-29	...modified crystal proteins having <b>one or more alterations</b> introduced...  ... the <b>mutagenesis of one or more</b> codons within the sequence of a toxin ...  ... mutations may also be made in insecticidal crystal proteins, including the <b>loop regions, helices regions</b> ...  ... Cry3Bb* variants ... that have <b>one or more changes</b> incorporated into the amino acid sequence of the protein ...
Page 23, lines 11-13;  Lines 15-18	... mutations in the amino acid sequences or underlying DNA gene sequences which result in the <b>insertion or deletion of one or more</b> amino acids ...  ... <b>mutate or delete one or more</b> nucleotides from the nucleic acid sequences of the genes encoding such polypeptides, or alternatively ... <b>add one or more nucleotides</b> into the primary nucleic acid sequence at <b>one or more sites</b> in the sequence ...
Page 29, lines 13-15	... introducing <b>one or more mutations</b> into the nucleic acid sequence to produce a <b>change in one or more amino acid residues</b> in the encoded polypeptide sequence ...
Page 41, lines 8-9	... the <i>cry3</i> * gene encodes an amino acid sequence in which <b>one or more amino acid residues have been changed</b> ...

In addition, Table 2 of the instant specification provides at least eight exemplary variants that are encompassed by the presently amended claim 44. The exemplary variants include Cry3Bb.11032, Cry3Bb.11035, Cry3Bb.11046, Cry3Bb.11057, Cry3Bb.11081, Cry3Bb.11082, Cry3Bb.11084 and Cry3Bb.11098, which variants have been reflected in presently added claim 53.

In view of the above remarks, Applicants believe that the phrase “one or more point mutations result in at least one amino acid substitution of Asp165 to Gly” as recited in the presently amended claim 44 is clearly and unambiguously supported by the instant specification.

As to mutations of Asp165 to Gly and one or more of the mutations at amino acids 311, 313 and 317, the Examiner states that each of variants 11082, 11098, 11081 and 11084 argued in Applicants’ previous response only provide support for the particular combination of substitutions made in those variants, and some of these variants have mutations other than those recited in the claim. In response, Applicants point out that claims 44-46, which refer to mutations of Asp165 to Gly and one or more of the mutations at amino acids 231, 311, 313, 317 and 348 recite the open-end language “comprises”. In particular, claim 46 refers to modified Cry3Bb\* polypeptides comprising (emphasis added) at least one substitution of Asp165 to Gly (in or near  $\alpha$  helix 4) as well as one or more substitutions at amino acid residues 231, 311, 313, 317 and 348, which feature is shared among the four variants 11082, 11098, 11081 and 11084. That is, these four variants indeed provide clear and unambiguous support to claims 44-46.

With respect to the phrase “one or more amino acid ... lysine or valine” in claim 40, Applicants submit that claim 40 has been amended to incorporate the subject matter of dependent claim 47. As amended, claim 40 refers to the one or more amino acid substitutions that are specifically exemplified in the instant specification. The specific exemplary variants of the

modified Cry3Bb\* polypeptides that are encompassed by presently amended claim 40 are listed in new claim 50.

In general, Applicants submit that the instant claims as presently amended refer to the modified Cry3Bb\* polypeptides comprising the one or more amino acid substitutions that are specifically exemplified in the instant specification. The specific variants that are encompassed by the presently amended claims are further claimed in new claims 50-54. For the Examiner's convenience, Applicants present the following Related Variant Table summarizing these specific variants. Applicants note that the below table is adapted from Table 2 of the instant specification.

**Related Variant Table**

<b>Variant</b>	<b>Amino Acid Changes</b>	<b>Structural Site of Changes</b>	<b>Claims Supported</b>
11032	D165G	$\alpha 4$	44, 45, 53
11035	S160N, K161P, R162H, D165G	$\alpha 4$	44, 45, 53
11046	S160N, K161P, R162H, D165G, I289V, S293P	$\alpha 4$ ; $1\alpha 7, \beta 1$	44, 45, 53
11057	D103E, $\Delta A104$ , S160N, K161P, R162H, D165G	$1\alpha 2a, 2b$ ; $\alpha 4$	44, 45, 53
11081	D165G, S311T, E317K	$\alpha 4$ ; $1\beta 1, \alpha 8$	40, 44-46, 53, 54
11082	D165G, I289V, S293P, F305S, S311A, L312V, Q316W, Q348R, V365A	$\alpha 4$ ; $1\alpha 7, \beta 1$ ; $\beta 1$ ; $1\beta 1, \alpha 8$ ; $\beta 2$ ; $\beta 3b$	44-46, 53, 54
11084	D165G, S311L	$\alpha 4$ ; $1\beta 1, \alpha 8$	44-46, 53, 54 40-43, 50
11098	D165G, H231R, S311L, N313T, E317K	$\alpha 4$ ; $\alpha 6$ , $1\beta 1$ , $\alpha 8$	44-46, 53, 54 40-43, 50 48, 51
11228	S311L, N313T, E317K	$1\beta 1, \alpha 8$	40-43, 50
11229	S311T, E317K, Y318C	$1\beta 1, \alpha 8$	40-43, 50
11231	H231R, S311L, N313T, E317K	$\alpha 6$ ; $1\beta 1, \alpha 8$	40-43, 50 48, 51, 52
11232	S311T, L312P, N313T, E317N	$1\beta 1, \alpha 8$	40-43, 50
11235	H231R, S311L	$\alpha 6$ ; $1\beta 1, \alpha 8$	40-43, 50 48, 51

In conclusion, Applicants believe that the present amendments are sufficient to overcome this written description rejection. As such, it is respectfully requested that the present rejection be removed.

**Rejection under 35 U.S.C. § 112, second paragraph**

Claims 47-49 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Examiner states that claim 47 lacks antecedent basis for the limitation "said one or more amino acid replacement". In response, Applicants submit that claim 47 has been cancelled. As such, this rejection is moot.

\*\*\*\*\*

This response is filed along with a petition for a one-month extension of time. The Commissioner is authorized to deduct the extension fee (\$120) from Howrey LLP Deposit Account No. 08-3038/11792.0218.DVUS01. Should any additional fees be required for any reason relating to this document, the Commissioner is authorized to deduct said fees from the same Deposit Account.

Respectfully submitted,



J. Wendy Davis, Ph.D.  
Reg. No. 46,393  
Agent for Assignee  
MONSANTO TECHNOLOGY LLC

Customer No. 45607  
HOWREY LLP  
1111 Louisiana, 25<sup>th</sup> Floor  
Houston, Texas 77002  
(713) 787-1512 (direct)

Date: July 25, 2006